actuations of said valve stem, and whereby said first and second volumes of said pharmaceutical product dispensed during said first and second actuations of said valve stem are substantially equal.

15. (New) A metered dose inhaler, comprising:

an aerosol container containing a drug and a hydrofluoroalkane propellant;

a valve stem having a dispensing channel, said dispensing channel being adapted to receive and expel a predetermined volume of said drug when said valve stem is actuated; and

a valve body having a metering chamber, said metering chamber including at least one metering chamber wall, said metering chamber being in communication with said dispensing channel during said actuation of said valve stem, said metering chamber being adapted to receive a first volume of said drug at a first time, dispense said first volume of said drug during a first actuation of said valve stem, receive a second volume of said drug at a second time and dispense said second volume of said drug during a second actuation of said valve stem, at least said metering chamber wall and said dispensing channel comprise a material selected from the group consisting of a fluorinated ethylene propylene, polytetrafluoroethylene, a copolymer of a polytetrafluoroethylene and combinations thereof, whereby substantially all of said first and second volumes of said drug are dispensed during said first and second actuations of said valve stem, and whereby said first and second volumes of said drug dispensed during said first and second actuations of said valve stem are substantially equal.

II. REMARKS

A. Introduction

Applicant submits this Response in a bona fide attempt to (i) advance the prosecution of this case, (ii) answer each and every ground of rejection as set forth by the Examiner, (iii) place the claims in a condition for allowance, and (iv) place the case in better condition for consideration on appeal. Applicant respectfully requests reexamination and reconsideration of the above referenced patent application in view of this Response.

As indicated above, Applicant has amended Claims 1 and 10. Applicant has also added new Claims 11 - 15.

Attached hereto is a marked-up version of the changes made to the claims by the current amendments. The attached page is captioned **"Version With Markings To Show Changes Made."**

Applicant respectfully submits that the noted amendments (and new claims) merely make explicit that which was (and is) disclosed or implicit in the original disclosure. The amendments thus add nothing that would not be reasonably apparent to a person of ordinary skill in the art to which the invention pertains.

B. Response to Rejections

The Examiner has rejected Claims 1 and 10 under 35 U.S.C. § 103(a) as being unpatentable over Digiovanni, et al. (WO 97/16360) in view of Cunningham (Pat. No. 3,709,410). The Examiner contends:

> "In column 3, line 1 to column 4, line 38, Digiovanni et al. teaches of a metering valve having a body (1) defining a metering chamber (2), seals (3,4), a spring (5) and a stem 10, made of PTFE. The propellant used in the dispenser is disclosed as HFA. Digiovanni et al. does not explicitly teach making any other part of the valve of PTFE. Cunningham teaches that it is known in the dispensing valve art to make a valve body of Teflon (PTFE). It is established that Teflon has the well known properties of being chemically non-reactive to a many materials and further to provide non-stick characteristics.
>
> It would have been obvious to one having ordinary skill in the art at the time of the invention to have made any of the valve structure parts, including the valve body and metering chamber of Digiovanni et al. out of PTFE as both Digiovanni et al. Cunningham teaches that it is known in the dispensing valve art to make various parts out of Teflon (PTFE) in order to take advantage of Teflon's well known properties such as enhanced chemical non-reactiveness and non-stick characteristics.
>
> Further, with respect to claim 10, the dispensing of drugs from a metering dose dispenser as show by Digiovanni et al. is well established in the dispensing art. It would have been obvious to one having ordinary skill in the art at the time of the invention to have selected the substance to be dispensed of Digiovanni et al. to be a drug in order to obtain the advantages of the Digiovanni et al. dispenser in dispensing a drug."

Applicant respectfully submits that the metering valve assembly and metered dose inhaler embodied in Claims 1 and 10, as amended, are unobvious over Digiovanni, et al., alone or in combination with any known reference.

In determining what is and what is not obvious under § 103, **all** properties and advantages **not** in the prior art must be considered. See *In re Wright*, 848 F.2d 1216, 6 U.S.P.Q. 2d 1959, 1962 (Fed. Cir. 1988) ("Factors including unexpected results, new features, solution of a different problem, novel properties, are all considerations in the determination of obviousness in terms of 35 U.S.C. § 103"). Indeed, it is the invention as a whole, including distinct functions that must be considered in obviousness determinations. Further, obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination. See *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577, 221 U.S.P.Q. 929, 922 (Fed. Cir. 1984).

As set forth above, Claims 1 and 10, as amended, provide for a metering valve assembly having (i) a valve stem with a dispensing channel that is adapted to receive and expel a predetermined volume of a pharmaceutical product when the valve stem is actuated and (ii) a valve body having a metering chamber that is in communication with the dispensing channel, the metering chamber being adapted to receive at least a first volume of said pharmaceutical product at a first time, dispense said first volume of said pharmaceutical product during a first actuation of said valve stem, receive a second volume of said pharmaceutical product at a second time and dispense said second volume of said pharmaceutical product during a second actuation of said valve stem, *the metering chamber comprising a material selected from the group consisting of a fluorinated ethylene propylene, a copolymer of a polytetrafluoroethylene and combinations thereof, whereby substantially all of the first and second volumes of the pharmaceutical product are dispensed during the first and second actuations of the valve stem, and whereby the first and second volumes of the pharmaceutical product dispensed during the first and second actuations of the valve stem are substantially equal.*

A key element of Applicant's metering valve assembly is thus the use of a fluorinated polymer to construct the metering chamber to remedy the problem of pharmaceutical product (or drug) deposition on the walls of the metering chamber, which Applicant has found to be a

primary source of dose variation and inconsistency. As set forth in the Specification:

> "[T]he invention allows one to make a metering valve in which the metering chamber 2 fills in a very precise manner after each actuation of the valve and the majority, if not the totality, of the contents of the metering chamber is expelled at each actuation such that the dose is very precise and reproducible."
> p. 6, ll. 13-16.

In the seminal case of *Eibel Process Co. v. Minnesota and Ontario Paper Co.*, 261 U.S. 45 (1923), the Court established the rule that the discovery of the source of a problem can result in a patentable invention despite the fact that the solution would have been obvious once the source of the problem was discovered. See also, *In re Peehs*, 612 F.2d 1287, 204 U.S.P.Q. 835 (CCPA 1980) ("A patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is *part* of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. §103.").

In the instant matter, not only did Applicant discover the source of a significant problem associated with metering valves and, hence, metered dose inhalers employing same, but, also discovered an effective solution to the problem. As discussed in detail below, neither Digiovanni, et al., nor Cunningham (i) recognized the problem or it source or (ii) taught or suggested Applicant's solution to the problem.

Indeed, Digiovanni, et al. discloses a metered dose inhaler having, *inter alia*, a metering chamber 2 and a valve plunger 10. The plunger 10 corresponds to the valve stem of the present invention. According to Digiovanni, et al:

> "To ensure that the metering valve operates, and in particular that the valve plunger returns from its actuation position to its rest position under drive from the spring 5, thereby avoiding 'sticking' problems, i.e., problems associated with said valve plunger jamming because of friction exerted by the valve gasket 3, the invention provides for the valve plunger 10 to be made of a material having improved friction qualities, i.e., that slides better over the sealing gaskets. For this reason, the invention provides for the valve plunger 10 to be made of a material comprising an acetal resin, polytetrafluoroethylene (PTFE), and silicon. More specifically, the acetal resin may be polyoxymethylene and the silicon may be present in the mixture in the form of silicon oil. Typically, a material made of polyoxymethylene constituting about 80% by weight, of PTFE constituting about 15% by

> weight, and of silicon oil constituting about 5% by weight is suitable for making the valve plunger of the invention." (emphasis added) Col. 3, line 59 - Col. 4, line 9.

Digiovanni, et al.'s valve plunger 10 thus comprises a mixture of acetal resin, PTFE and silicon. The noted mixture is employed to remedy a totally different problem associated with some metering valves, i.e., "sticking valves".

Digiovanni, et al. is devoid of any reference to or mention of pharmaceutical product deposition on the walls of a metering chamber and the resulting dose of a pharmaceutical product that is dispensed from the metering chamber. Moreover, and most significantly, Digiovanni, et al. does not teach or suggest a "metering chamber" that solely comprises fluorinated ethylene propylene, a copolymer of a polytetrafluoroethylene and/or a combination thereof to provide precise and reproducable metered doses of a pharmaceutical product to a patient.

Cunningham merely discloses an aerosol valve having a uni-directional, pressure-actuated, expanding slot valve body. During a "pressure fill" operation, aerosol product flows through the valve interior defined by the valve body 20 and into a container. (Col. 3, ll. 43-49 and Col. 4, line 28).

The problem addressed by the Cunningham aerosol valve is the low filling rates that are often associated with aerosol valves having small orifice sizes. Cunningham is thus similarly devoid of any reference to or mention of pharmaceutical product deposition on the walls of a metering chamber and the resulting dose of a pharmaceutical product that is dispensed from the metering chamber.

Further, the valve body 20 disclosed by Cunningham does not include a metering chamber that is adapted to continuously receive and dispense a predetermined volume of a pharmaceutical product. Thus, Cunningham similarly does not teach or suggest a "metering chamber" that solely comprises fluorinated ethylene propylene, a copolymer of a polytetrafluoroethylene and/or a combination thereof to provide precise and reproducible metered doses of a pharmaceutical product to a patient.

Additionally, according to Cunningham, the valve body 20 "may be made of a plastic material such as nylon, teflon, polystyrene, ABS, acrylic, phenolic or vinyl resin." Col. 3, ll. 50-52. As is well known in the art, each of the noted materials has a unique surface characteristic/feature, particularly, surface affinity. Indeed, with the exception of Teflon, a

pharmaceutical product could, and in many instances would, tend to adhere to or react with the surface of a metering chamber that is constructed of the materials disclosed in Cunningham.

Applicant thus respectfully submits that Claims 1 and 10, and new Claims 11-15 define an invention that is unobvious over the cited references. Claims 1-15 should thus be deemed allowable.

Applicant has also reviewed the prior art made of record and not relied upon by the Examiner and has found them not to teach or make obvious the present invention.

III. CONCLUSION

Applicant having answered each and every ground of rejection as set forth by the Examiner, and having added no new matter, believes that this response clearly overcomes the references of record, and now submits that all claims in the above-referenced patent application are in condition for allowance and the same is respectfully solicited.

Respectfully submitted,
GlaxoSmithKline

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I hereby certify that this document is being deposited with the United States Postal Service on this date 12-02-02 in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EV121438090US addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Danielle Gragg
Name of person mailing document

Danielle Gragg

VERSION WITH MARKINGS TO SHOW CHANGES

In the claims:

Claims 1 and 10 have been amended as follows:

1. (3X Amended) A metering valve assembly for dispensing a pharmaceutical product, comprising:

a valve stem having a dispensing channel, said dispensing channel being adapted to receive and expel a predetermined volume of said pharmaceutical product when said valve stem is actuated; and

a valve body [constructed from] having a metering chamber, said metering chamber including at least one metering chamber wall, said metering chamber being in communication with said dispensing channel during said actuation of said valve stem, said metering chamber being adapted to receive a first volume of said pharmaceutical product at a first time, dispense said first volume of said pharmaceutical product during a first actuation of said valve stem, receive a second volume of said pharmaceutical product at a second time and dispense said second volume of said pharmaceutical product during a second actuation of said valve stem, at least said metering chamber wall comprising a material selected from the group consisting of a fluorinated ethylene propylene, polytetrafluoroethylene, a copolymer of a polytetrafluoroethylene and combinations thereof, [wherein the valve body defines a metering chamber, one or more seals, a valve stem, and a spring] whereby substantially all of said first and second volumes of said pharmaceutical product are dispensed during said first and second actuations of said valve stem, and whereby said first and second volumes of said pharmaceutical product dispensed during said first and second actuations of said valve stem are substantially equal.

10. (3X Amended) A metered dose inhaler, comprising:

an aerosol container containing a drug and a hydrofluoroalkane propellant[,];

a valve stem having a dispensing channel, said dispensing channel being adapted to receive and expel a predetermined volume of said drug when said valve stem is actuated; and

a valve body [constructed from] having a metering chamber, said metering chamber including at least one metering chamber wall, said metering chamber being in communication with said dispensing channel during said actuation of said valve stem, said metering chamber being adapted to receive a first volume of said drug at a first time, dispense said first volume of said drug during a first actuation of said valve stem, receive a second volume of said drug at a

second time and dispense said second volume of said drug during a second actuation of said valve stem, at least said metering chamber wall comprising a material selected from the group consisting of a fluorinated ethylene propylene, polytetrafluoroethylene, a copolymer of a polytetrafluoroethylene and combinations thereof, [wherein the valve body defines a metering chamber, a valve stem, one or more seals, and a spring] whereby substantially all of said first and second volumes of said drug are dispensed during said first and second actuations of said valve stem, and whereby said first and second volumes of said drug dispensed during said first and second actuations of said valve stem are substantially equal.

Claims 11 – 15 have been added.

11. (New) The metering valve assembly of Claim 1, wherein said metering valve assembly includes at least one metering chamber seal disposed proximate said metering chamber.

12. (New) The metering valve assembly of Claim 1, wherein said metering valve assembly includes at least one elastic component in communication with at least said valve stem.

13. (New) The metering valve assembly of Claim 12, wherein said elastic component comprises a spring.

14. (New) A metering valve assembly for dispensing a pharmaceutical product, comprising:

a valve stem having a dispensing channel, said dispensing channel being adapted to receive and expel a predetermined volume of said pharmaceutical product when said valve stem is actuated; and

a valve body having a metering chamber, said metering chamber including at least one metering chamber wall, said metering chamber being in communication with said dispensing channel during said actuation of said valve stem, said metering chamber being adapted to receive a first volume of said pharmaceutical product at a first time, dispense said first volume of said pharmaceutical product during a first actuation of said valve stem, receive a second volume of said pharmaceutical product at a second time and dispense said second volume of said pharmaceutical product during a second actuation of said valve stem, at least said metering chamber wall and said dispensing channel comprise a material selected from the group consisting of a fluorinated ethylene propylene, polytetrafluoroethylene, a copolymer of a polytetrafluoroethylene and combinations thereof, whereby substantially all of said first and

second volumes of said pharmaceutical product are dispensed during said first and second actuations of said valve stem, and whereby said first and second volumes of said pharmaceutical product dispensed during said first and second actuations of said valve stem are substantially equal.

15. (New) A metered dose inhaler, comprising:

an aerosol container containing a drug and a hydrofluoroalkane propellant;

a valve stem having a dispensing channel, said dispensing channel being adapted to receive and expel a predetermined volume of said drug when said valve stem is actuated; and

a valve body having a metering chamber, said metering chamber including at least one metering chamber wall, said metering chamber being in communication with said dispensing channel during said actuation of said valve stem, said metering chamber being adapted to receive a first volume of said drug at a first time, dispense said first volume of said drug during a first actuation of said valve stem, receive a second volume of said drug at a second time and dispense said second volume of said drug during a second actuation of said valve stem, at least said metering chamber wall and said dispensing channel comprise a material selected from the group consisting of a fluorinated ethyléne propylene, polytetrafluoroethylene, a copolymer of a polytetrafluoroethylene and combinations thereof, whereby substantially all of said first and second volumes of said drug are dispensed during said first and second actuations of said valve stem, and whereby said first and second volumes of said drug dispensed during said first and second actuations of said valve stem are substantially equal.